

REMARKS

Claims 1-10, 23-38, 40-42, 44, 45, 47 and 63-68 are pending and under consideration in the present application.

In the Office Action of March 9, 2004, the Office rejected claims 1-10, 23-38, 40-42, 44, 45, 47 and 63-68 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Zouboulis et al. (Dermatology 196) or Rosenfield (6,004,751) in view of Bryan (Crit. Rev. Onc. 5(4)). This rejection is respectfully traversed for the reasons set forth below. Reconsideration is respectfully requested.

The burden of establishing a prima facie case of obviousness lies with the Examiner. In determining obviousness, one must focus on the invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 U.S.P.Q. 2d 1241, 1246 (Fed. Cir. 1991). The primary inquiry is: "Whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success.... Both the suggestion and the expectation of success must be found in the prior art, not the applicant's disclosure." *In re Dow Chemical Co.*, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988).

A prior art reference must be considered in its entirety, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed. Cir. 1983); M.P.E.P. 2141.02. "Furthermore, the totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. *In re Hedges*, 228 U.S.P.Q. 685 (Fed. Cir. 1986); M.P.E.P. 2145. "In determining whether such a suggestion can fairly be gleaned from the prior art, the full field of

the invention must be considered for the person of ordinary skill is charged with knowledge of the entire body of technological literature, including that which might lead away from the claimed invention.” *In re Dow Chemical Co.*, 5 U.S.P.Q.2d at 1529 (Fed. Cir. 1988).

The Applicant respectfully submits that the Office has not set forth a prima facie case of obviousness as discussed below.

Rosenfield is directed to the cultivation of cells of the preputial gland derived from a transgenic mouse homozygous for a temperature sensitive strain of SV40T (cf. Example IV), while Zouboulis et al. (Dermatology 196) is directed to the use of non-immortalized human sebocytes for the research on seborrhoea and acne. Bryan is generally directed to the immortalization of different human cell types using SV40T.

In contrast to the cells according to the present invention, the cells according to Rosenfield are not produced by *in vitro* transfection of the SV40T gene. Hence, Rosenfield does not teach or suggest the present invention. Moreover, the cells of the preputial gland described in Rosenfield are only a model for the study of human sebaceous cells. In fact, cells of the preputial gland were used before the present invention was made due to the lack of an immortalized human sebaceous cell line. Cells of the preputial gland are not “sebocytes” as used in the present invention. For example, in D. Thiboutot et al., J. Invest. Dermatol. 115:614 (2000), the use of preputial cells as a model for human sebocytes is described (at page 618, right column, 2nd paragraph). As such, the cells of Rosenfield are different from the cells of the present application.

In addition, since the skin diseases acne and seborrhea are exclusively related to humans, the animal cells used as a model for studying these diseases clearly have disadvantages compared to the human cells of the present invention, as the human cells are involved in the concrete pathological mechanism. Rosenfield discloses cells of the preputial gland derived from a transgenic mouse and, therefore, does not teach or suggest the present invention.

Zouboulis et al. (Dermatology 196) is directed to the use of non-immortalized human sebocytes for the research on seborrhoea and acne. With regards to Zouboulis et al., it should be pointed out that the immortalization of human epithelial cells with DNA coding for virus proteins, in contrast to the immortalization of , e.g., fibroblasts, is a very complicated and difficult process. It is especially difficult to immortalize specialized human epithelial cells such as sebocytes. A particular problem in immortalizing epithelial cells is the fact that some SV40-established cell lines lose their differentiated properties and change their phenotype, i.e., they lose their typical characteristics and are not suitable for the purpose of the present invention (see, Bryan, page 339, right column). In contrast to the change of phenotype due to the immortalization with SV40T described in the cited prior art, the cell line according to the present invention still exhibits all typical sebocyte properties (at, for example, the specification, page 7, second paragraph). In order to further emphasize the difficulties in this regard, the publication Jiang et al., "Comparison of Methods for Transfection of Human Epidermal Keratinocytes," J. Invest. Dermatol. 97:969 (1991) is of interest, wherein different transfection methods are compared and where the problem of a loss of differentiation is also mentioned (at, e.g., page 969). Thus, Zouboulis et al. does not teach or suggest the present invention.

In addition, unlike other endo- and epithelial cells, human sebocytes in the body and in culture are “programmed” to differentiate and die in a short period, making it difficult to culture even primary sebocytes (see specification, at, e.g., page 3, first paragraph). Accordingly, the immortalization of human sebocytes without losing their differentiation was not obvious to one ordinarily skilled in the art at the time of the invention.

Bryan is generally directed to the immortalization of different human cell types using SV40T. Bryan does not teach or suggest an immortalized sebocyte and in fact, teaches away from the present invention as discussed *supra*. Furthermore, the Office does not establish any reason, suggestion, or motivation to combine Zouboulis or Rosenfield and Bryan as required to establish a *prima facie* case of obviousness. For example, the Board of Patent Appeals and Interferences overturned the Office’s obviousness rejection of claims to a human cell line cloned from a cell stably transformed by a recombinant vector comprising a reporter gene operatively linked to a human IL-4-responsive element in view of a reference disclosing the recombinant vector and transfection of human cells with the vector using the DEAE-dextran method combined with references teaching the use of the DEAE-dextran method for the stable transformation of cells, where the references did not teach or suggest “the making of a stably transformed cell expressing this vector.” *Ex parte Vries et al.*, Appeal No. 1996-3797, B.P.A.I. (1996) (unpublished). In this decision, the Board stated:

To establish a *prima facie* case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed subject matter. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required.

That knowledge cannot come from the applicants' disclosure of the invention itself.

Id., at page 7, citing *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 678-79, 7 U.S.P.Q.2d 1315, 1318 (Fed. Cir. 1988); *In re Geiger*, 815 F.2d 686, 688, 2 U.S.P.Q.2d 1276, 1278 (Fed. Cir. 1987); *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143, 227 U.S.P.Q. 543, 551 (Fed. Cir. 1985).

Furthermore, it was unexpected that the Applicant could successfully obtain immortalized sebocytes suitable for the intended use as described in the present invention. The objective problem underlying the present invention is to provide a human immortalized sebocyte culture having substantially the same properties as a primary sebocyte culture suitable for further investigations in the field of sebocyte-related human skin diseases. This problem is surprisingly solved by the inventive sebocytes. In view of the cited documents, it is apparent that none of these documents or a combination of these documents is able to teach or suggest the present invention. Hence, the present invention is not obvious in view of any of these documents.

Finally, it should be noted that although there was still a strong international need for an immortalized human sebocyte cell line, merely one other scientific group has succeeded, after the priority date of the present application, in the establishment of such a cell line using the method disclosed in the present invention. This clearly shows the outstanding quality and uniqueness of the cell line according to the present invention.

In view of the above, Applicant submits that the rejection of claims 1-10, 23-38, 40-42, 44, 45, 47 and 63-68 under 35 U.S.C. § 103(a) as allegedly obvious over Zouboulis et al.

(Dermatology 196) or Rosenfield (6,004,751) in view of Bryan (Crit. Rev. Onc. 5(4)) is improper and should be withdrawn.


CONCLUSION

It is respectfully submitted that entry of this Response will place the claims in condition for Allowance. Applicant requests early and favorable notice to that effect.

The Examiner is encouraged to contact the undersigned with any questions or to otherwise expedite prosecution.

Respectfully submitted,

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